

# Novel therapy of AKI

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# Treatment of AKI

## **Aims of treatment:**

1. Maintenance of Fluid and Electrolyte Homeostasis
2. Preventing Life-threatening Complications
3. Avoiding Further Kidney Injury
4. Providing Appropriate Nutrition
5. RRT in most severe forms of AKI





**Therapy to Decrease injury and promote Recovery**

Renal dose dopamine....

Endothelin antibodies

No human trials

Thyroxine

More rapid improvement of renal function in animals

Increased uptake of ADP to form ATP or cell membrane stabilization as a possible cause

- ANP

an atrial natriuretic peptide, it increases the GFR by dilating afferent arterioles while constricting efferent arterioles and so improve GFR , urinary out put .

- Improve renal function and decrease renal insufficiency
- ? Nesiritide role

- Theophylline

- Adenosine antagonist – prevents reduction in GFR.

- Growth Factors

- After ischemic insult, infusion of IGF-I, Epidermal GF, Hepatocyte GF improved GFR, diminished morphologic injury, diminished mortality

- None of these things are well tested.....

administration of melatonin-stimulating hormone, C5a receptor antagonist, selective inhibitors of inducible nitric oxide synthase, statins & novel inhibitor of the Na / H exchange subtype 3 as well as inhibition of monocyte chemoattractant protein 1 by gene therapy has been shown to ameliorate AKI

other studies demonstrate that anti-adhesion molecule therapy markedly decrease ischemic renal injury by preventing adhesion of activated neutrophils to renal cells.



# Is there a role for Fenoldopam in prevention or treatment of AKI in ICU setting?

Dopamine-1 receptor agonist, lack of Dopamine-2, and alpha-1 receptor effect, make it a potentially safer drug than Dopamine!

Reduces in hospital mortality and the need for RRT in AKI

Reverses renal hypoperfusion more effectively than renal dose Dopamine

*J Cardiothorac Vasc Anesth.* 2008 Feb;22(1):23-6.

*J Cardiothorac Vasc Anesth.* 2007 Dec;21(6):847-50

*Am J Kidney Dis.* 2007 Jan;40(1):56-68

*Crit Care Med.* 2006 Mar;34(3):707-14

# NAC

The most recent trials seem to confirm a potential positive preventive effect of *N*-acetylcysteine (NAC), particularly in contrast-induced nephropathy (CIN. (150 mg/kg in 500 mL saline (0.9%)] over 30 min immediately before contrast exposure and followed by 50 mg/kg in 500 mL saline (0.9%) over the subsequent 4 h )

# EPO

Erythropoietin (EPO) has tissue-protective effects and prevents tissue damage during ischaemia and inflammation, and currently trials are performed with EPO in the prevention of AKI post-cardiac surgery, CIN and post-kidney transplantation.

# **Protective Effect of Ginsenoside against Acute Renal Failure and Expression of Tyrosine Hydroxylase in the Locus Coeruleus**

**H. A. ZHANG<sup>1</sup>, M. WANG<sup>1</sup>, J. ZHOU<sup>1</sup>, Q. Y. YAO<sup>1</sup>, J. M. MA<sup>2</sup>, C. L. JIANG<sup>1</sup>**

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the treatment of ARF rats with ginsenosides for 48 h significantly reduced the serum blood urea nitrogen, creatinine level, and lipid peroxidation

the question whether there is a correlation between the renal protective effect of ginsenosides against acute renal failure and the activation of tyrosine hydroxylase in the locus coeruleus

# **Reversal of acute renal failure by bortezomib-based chemotherapy in patients with multiple myeloma**

Heinz Ludwig, Johannes Drach, Helmut Graf, Alois Lang, Johannes Gobertus Meran

haematologica/the hematology journal | 2007; 92(10)

the use of bortezomib-based treatment in patients with acute renal failure with the intention to achieve a rapid reduction of light chains and to reverse renal Impairment



## **NOVEL SUBSTRATES**

- The use of novel substrates in acute illness to modulate the stress response is an area of research that is expanding. Glutamine, recognised as a conditionally essential amino acid, has many functions.

- One of its major roles is as an oxidative substrate for rapidly replicating cells, such as the gastrointestinal mucosal cells and immune cells – lymphocytes and macrophages.

# DIALYSIS

- CRRT Versus IHD
- CRRT Versus EDD
- PD Versus CRRT

# ADVANTAGES OF CRRT

- ✖. In these patients, continuous renal replacement therapy (CRRT) is used because
  - ✖ it allows a slow, moderate blood purification process to reduce the patient's burden.
  - ✖ CRRT is indicated in patients with severe acute pancreatitis, fulminant hepatitis, postoperative liver failure, multiple organ failure, cardiovascular disease, and severe renal failure.
  - ✖ CRRT is provided mainly in critical care and intensive care units..

CRRT has several disadvantages, including intensive nursing requirements, continuous anticoagulation, patient immobility, and expense.

There was no difference in mortality. The EDD eliminated the need for constant supervision of the equipment while allowing 1 nurse to manage more than one treatment

It is significantly less complex and costly than CRRT and obviates the need for anticoagulation, making PD a popular method for the treatment of ARF in developing countries



however, is a potential source of complications such as catheter leaks and peritonitis. Albumin losses through the peritoneal membrane can also be significant. In addition, the decreased splanchnic perfusion in states of shock and sepsis may impair solute exchange and volume removal by PD.

# The Bioartificial Kidney

- This novel adjunctive extracorporeal device consists of a hemofilter, followed in series by a renal tubular cell-lined hollow-fiber membrane apparatus
- it alters cytokine levels favorably and improves hemodynamic parameters including MAP and cardiac output

# Dialyzer Characteristics

# Stem cell therapy

# Pathfinder Cells Provide A Novel Therapeutic Intervention For Acute Kidney Injury

Liane M. McGlynn,<sup>1</sup> Kathrin Eller,<sup>2,3</sup> Alasdair I. MacDonald,<sup>1</sup> Alan MacIntyre,<sup>1</sup> David Russell,<sup>4</sup>  
Christian Koppelstaetter,<sup>2</sup> R.W. Davies,<sup>1</sup> and Paul G. Shiels<sup>1</sup>

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- Pathfinder cells (PCs) are a novel class of adult-derived cells that facilitate functional repair of host tissue.'
- the use of PCs to regenerate damaged tissues and also offers a novel therapeutic intervention for repair of solid organ damage in situ

# Intravenous cell therapy for acute renal failure with serum amyloid A protein-reprogrammed cells

**Katherine J. Kelly,<sup>1</sup> Barbara Kluve-Beckerman,<sup>2</sup> Jizhong Zhang,<sup>1</sup> and Jesus H. Dominguez<sup>1,3</sup>**

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- Learning without thought is labour lost;  
thought without learning is perilous.  
(*Confucian Analects*)





**THANK YOU**

**Any questions???**